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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,453	11/22/2004	William Herman	HER1-006	9409

62879 7590 11/06/2006

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/501,453	HERMAN, WILLIAM	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *One* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2004*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

I. Claims 1-20 are pending.

Election/Restrictions

II. Restriction to one of the following inventions is required under 35 U.S.C. 121 and 372:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1:

1. Claims 10, 13, and 18, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said **first ligand is a specific CD cell surface marker other than CD4**, and said second ligand is **CCR5**.

2. Claims 10, 13, and 18, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is a specific **CD cell surface marker other than CD4** , and said second ligand is **CXCR4**.

3. Claims 11, 13-15, and 18, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and

selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is a specific **CD4** cell surface marker, and said second ligand is **CCR5**.

4. Claims 11, 13-15, and 18, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is a specific **CD cell surface marker other than CD4** , and said second ligand is **CXCR4**.

5. Claims 12 and 13, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is **a specific cell surface marker associated with cancer cell or pre-cancerous cell**, and said second ligand is **CCR5**.

6. Claims 12 and 13, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is **a specific cell surface marker associated with cancer cell or pre-cancerous cell**, and said second ligand is **CXCR4**.

7. Claims 13 and 15, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is a specific cell surface marker associated with a **specific autoimmune disease or rheumatic disease other than CD4**, and said second ligand is **CCR5**.

8. Claims 13 and 15, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is a specific cell surface marker associated with **specific autoimmune disease or rheumatic disease other than CD4**, and said second ligand is **CXCR4**.

9. Claims 13, 16, and 18, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is **a specific cell surface marker associated with a specific tissue type**, or class and said second ligand is **CCR5**.

10. Claims 13, 16, and 18, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds

to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is **a specific cell surface marker associated with a specific tissue type**, or class, and said second ligand is **CXCR4**.

11. Claims 13 and 17, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is **a specific cell surface marker associated with a specific organ**, and said second ligand is **CCR5**.

12. Claims 13 and 17, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is **a specific cell surface marker associated with a specific organ**, and said second ligand is **CXCR4**.

13. Claims 13 and 19, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is **a specific cell surface marker associated with MHC-peptide complex**, and said second ligand is **CCR5**.

14. Claims 13 and 19, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is **a specific cell surface marker associated with MHC-peptide complex**, and said second ligand is **CXCR4**.

15. Claims 13 and 20, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is **a specific cell surface marker associated with a cell surface immunoglobulin**, and said second ligand is **CCR5**.

16. Claims 13 and 20, drawn to a composition comprising a multispecific ligand comprising at least a first ligand binding, moiety which specifically binds to a first ligand having a first biodistribution and a second ligand binding moiety which specifically binds to a second ligand having a second biodistribution different from that of the first ligand, and wherein the affinity of the first and second ligand binding moieties are different and selected to bias the biodistribution of the multispecific ligand, the multispecific ligand is a **bispecific antibody**, said first ligand is **a specific cell surface marker associated with a cell surface immunoglobulin**, and said second ligand is **CXCR4**.

The inventions listed as Groups 1-16 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The US Pat No 6,319,675 (filed Nov 24, 1999; PTO 892) teaches a composition comprising a multispecific ligand such as bispecific antibody comprising a first binding moiety

such as antibody or binding fragment thereof that binds specifically to a first ligand such as Bonzo (also known as CXCR5) or a ligand to Bonzo and a second ligand such as antibody or binding fragment thereof that binds to a second ligand such as CD30 expressed on a target cell or carcinoembrionic antigen associated with cancer cell or precancerous cell (see col. 20, lines 55-67, col. 23, lines 1-39, in particular). The affinity of the reference antibody or binding fragment thereof that binds specifically Bonzo with high affinity such as about 1000, or 100 or within a factor of 10, which inherently bias the biodistribution of the reference multispecific ligand (see col. 24, lines 15-32, in particular). The reference composition further comprises a physiological acceptable excipient such as phosphate-buffered saline (see col. 35, line 48-67, in particular).

Since Applicant's inventions do not contribute a special technical feature when viewed over the prior art they do not have single general inventive concept and lack unity of invention.

Linking claims 1-9 will be examined along with the elected Group if any one of Group 1-16 is elected. Claims 1-9 link inventions 1-16. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 1-9.

Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

III. Accordingly, Groups 1-16 are not so linked as to form a single general inventive concept and restriction is proper.

IV. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

V. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until all claims to the elected product claim are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

VI. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

VII. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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